

Application No.: 09/932,676

Docket No.: NCI-006DV2

**REMARKS/ARGUMENTS**

Claims 68-90 are pending in the instant application. *No new matter has been added.*

Amendment and/or cancellation of the claims during the prosecution of the instant application are not to be construed as acquiescence to any of the objections/rejections set forth in the instant Office Action or any previous Office Action, and were done solely to expedite prosecution of the application. Applicants submit that claims were not added or amended during the prosecution of the instant application for reasons related to patentability. Applicants reserve the right to pursue the claims as originally filed, or similar claims, in this or one or more subsequent patent applications.

***Claim Rejections - 35 U.S.C. §103*****Rejection of Claims 88-90 under 35 U.S.C. §103(a)**

Claims 88-90 are rejected under 35 U.S.C. §103(a) as being unpatentable over El Nasser Ossman *et al.*, Chem. Abstract 107:168619. In particular, the Office Action states that "the reference teaches 2,4-quinazolidione compounds having anticonvulsant activity." The Office Action further states that instant claim 88

...excludes the reference disclosed compounds by the proviso statement, however, includes compounds wherein the ring nitrogen is substituted by H in place of the methyl ... or a propyl in place of the ethyl ..., etc.

The Office Action suggests "the instant claims include compounds that are homologs (i.e., differing by a -CH<sub>2</sub>- group) of the reference compounds," and that "compounds that are structurally homologous to prior art compounds are prima facie obvious, absent a showing of unexpected results. *In re Huas*, 60 USPQ 544 (CCPA 1944); *In re Henze*, 85 USPQ 261 (CCPA 1950)."

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Applicants respectfully traverse this rejection. Applicants submit that it is unclear how the prior art species listed in the attachment to the Office Action make the entire genus structure of claim 88 or dependent claims thereto, obvious; or how the entire genus structure is a homolog of a limited number of species, in accordance with the definition described in MPEP § 2144.09. Applicants also submit that suggesting that a species that is not encompassed by a claimed generic structure makes obvious the entire generic structure, appears incongruent with MPEP § 2144.09. Furthermore, Applicants respectfully point out the language of MPEP § 2144.09, which states that "...homologs which are far removed from adjacent homologs may not be expected to have similar properties." This language clearly indicates that a genus structure, which is not confined to adjacent homologs, is not prima facie obvious in light of a prior art species. As the instant claims are not confined to the adjacent homologs of the species disclosed in El Nasser Ossman *et al.*, Applicants submit that the genus structure is not prima facie obvious in light of the prior art species.

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Applicants also respectfully remind the Examiner of the factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a), which are summarized as follows:

- (1) Determining the scope and contents of the prior art.
- (2) Ascertaining the differences between the prior art and the claims at issue.
- (3) Resolving the level of ordinary skill in the pertinent art.
- (4) Considering objective evidence present in the application indicating obviousness or nonobviousness.

In this regard, (1) the Office Action has determined that the scope of the prior art falls within the four corners of the disclosure of El Nasser Ossman *et al.* As acknowledged by the Examiner, the relevant content of the prior art disclosure is limited to five species (recited therein), and the Examiner has agreed that such species have been removed from the scope of the claims by proviso.

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Accordingly, (2) *the difference between the prior art and the pending claims at issue is the entire claimed invention*. In fact, no part of the prior art reference recites subject matter that falls within the scope of the claims of the instant application, let alone that would make the entire scope of the rejected claims obvious. (3) The level of ordinary skill in the pertinent art has not been relied upon by the Examiner, and as such, has not been resolved in the instant Office Action. However, Applicants submit the ordinarily skilled artisan would not have been in the possession of the entire claimed invention by the teachings of the prior art in conjunction with the level of ordinary skill in the pertinent art at the time the invention was made.

Moreover, Applicants respectfully point out that as required by U.S.C. §103(a), the Examiner must demonstrate that

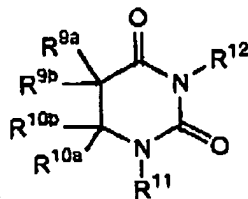
...the differences between the subject matter sought to be patented and the prior art are such that *the subject matter as a whole* would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains...(Emphasis added)

In this respect, the Office Action has failed to show that the entire claim is obvious in light of the prior art reference, nor to provide any additional prior art references, nor to indicate the skill in the art, which would make up for the deficiencies of the cited reference, *i.e.*, the Examiner has not shown that each and every element of the claimed invention is obvious in light of the supplied reference. Therefore, the Office Action has failed to provide a reference that would render obvious *the subject matter as a whole*. Furthermore, for convenience, Applicants present "The subject matter as a whole," *e.g.*, claim 88, below:

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Claim 88. A method for treating a convulsive disorder, comprising administering to a subject in need thereof an effective amount of a compound represented by the formula:



, wherein

$R^{9a}$ ,  $R^{9b}$ ,  $R^{10a}$ ,  $R^{10b}$  are each independently hydrogen, an alkyl, alkenyl, alkynyl, aryl, alkoxy, aryloxy, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, aryloxy carbonyl, amino, hydroxy, thiol, alkylthiol, nitro, cyano, halogen, carboxyl, alkoxycarbonyloxy, aryloxy carbonyloxy, or aminocarbonyl group, or one of  $R^{9a}$  and  $R^{9b}$  and one of  $R^{10a}$  and  $R^{10b}$  are both taken together and form a double bond; or

$R^{9a}$  and  $R^{9b}$ , together with the two-carbon unit to which they are attached, are joined to form a carbocyclic or heterocyclic ring having from 4 to 8 members in the ring;

$R^{10a}$  and  $R^{10b}$ , together with the two-carbon unit to which they are attached, are joined to form a carbocyclic or heterocyclic ring having from 4 to 8 members in the ring; or one of  $R^{9a}$  and  $R^{9b}$  is joined with one of  $R^{10a}$  and  $R^{10b}$ , together with the two-carbon unit to which they are attached, to form a carbocyclic or heterocyclic ring having from 4 to 8 members in the ring;

$R^{11}$  is hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylcarbonyl, arylcarbonyl, alkoxycarbonyl, or aryloxy carbonyl; or one of  $R^{10a}$  and  $R^{10b}$  is joined with  $R^{11}$ , together with the carbon atom and nitrogen atom to which they are respectively attached, to form a heterocyclic ring having from 4 to 8 members in the ring; and

$R^{12}$  is selected from the group consisting of hydrogen, alkyl, aryl and a carbohydrate;

or a pharmaceutically acceptable salt thereof; such that said convulsive disorder is treated, wherein the compound is not (1-ethyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl)-acetic acid ethyl ester, (1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl)-acetic acid ethyl ester, N-methyl-2-(1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl)-acetamide, N-benzyl-2-(1-methyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl)-acetamide, or (1-ethyl-2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl)-acetic acid (3-chloro-benzylidene)-hydrazide.

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Applicants submit that it should be clear from this claim (and those claims dependent upon this claim, *i.e.*, claims 88 and 89) that the difference between the five compounds of El Nasser Ossman *et al.* and the instantly claimed invention is the entire claimed invention.

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Accordingly, based on the foregoing arguments, Applicants respectfully request withdrawal of the rejection of claims 88-90 under 35 U.S.C. §103(a) and favorable reconsideration.

Formal Objection to Improper Finality

Furthermore, Applicants formally object to the finality of the Office Action, and request withdrawal of the finality. Applicants respectfully submit that the rejection of claims 88-90 under 35 U.S.C. §103(a) as being unpatentable over El Nasser Ossman *et al.*, Chem. Abstract 107:168619 was not necessitated by Applicants' amendment of the claims in response to the prior Office Action of April 18, 2003 (Paper No. 9), *i.e.*, as required by MPEP § 706.07(a). In particular, Applicants assert that such a rejection was available to the Examiner prior to the amendments and submit that, as such, the imposition of finality for the outstanding Office Action is improper. Accordingly, Applicants preserve their right to petition the finality of the instant Office Action under 37 C.F.R. 1.181 and M.P.E.P. §1002.02(c).

Applicants further request, upon the withdrawal of the finality of the Office Action that the present response be treated as a response to a non-final Office Action.

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***Provisional Rejection of Claim:  
Judicially Created Doctrine of Obviousness-Type Double Patenting***

**Provisional Rejection of Claim 68-90 under Judicially Created Doctrine of Obviousness-Type Double Patenting**

Claims 68-90 remain provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 68, 138 and 143-153 of copending Application No. 09/932,677. Moreover, the Office Action of April 18, 2003 (Paper No. 9) asserts that while the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims substantially overlap the reference claims. In particular, Paper No. 9 states that

[t]he reference method is drawn to administering compounds having an amino group (  $-NR^aR^b$  wherein  $R^a$  and  $R^b$  together form a substituted heterocycle) attached to a two carbon spacer carrying an anionic group...[and] one of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole.

Applicants traverse this rejection and respectfully submit that this rejection is improper in light of the Restriction Requirement issued by the United States Patent and Trademark Office in the mutual priority application (from which both applications have been derived as divisional applications). At this point, Applicants make the relevant notation that both the reference application and the present application are divisional applications of U.S. Utility Application 09/041,371 ("Parent Applications"), filed on March 11, 1998, and now issued as U.S. Patent No. 6,306,909.

Applicants specifically invite the Examiner's attention to the Restriction Requirement of the Parent Application (Paper No. 6) mailed from the United States Patent and Trademark Office on April 5, 1999. In particular, Applicants respectfully point out that the subject matter of claims 68-

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90 of U.S. Application No. 09/932,676 was the subject of claims 64-65 and 67, as well as claim 66, in the Parent Application, which were restricted as Group XII and Group XIII, respectively. Furthermore, in the Office Action of the Parent Application dated August 27, 1999 (Paper No. 10), the Examiner states on page 2 that

... the pending claims are drawn to noncyclic and cyclic  $\beta$ -amino acids. They are structurally dissimilar such that a reference anticipating a compound may not render the remaining compounds obvious. Note in the instant case, the reference anticipating the compounds according to the elected invention, does not render compounds according to other groups obvious.

Applicants note that Group III, drawn to noncyclic  $\beta$ -amino acids, was elected by Applicants in the Parent Application, and that such compounds were explicitly (at least, for example, by the statement above) considered patentably distinct from cyclic  $\beta$ -amino acids. Furthermore, Applicants respectfully remind the Examiner that the pending claims of the present application are drawn to cyclic  $\beta$ -amino acids, while the claims of the reference application are noncyclic  $\beta$ -amino acids. As such, the Examiner, by virtue of the Examiner's own language, has deemed these compounds patentably distinct.

Applicants respectfully point out that it is improper to reject claims under obviousness-type double patenting that were restricted out of a mutual parent application (from which each of the applications are derived as divisional applications of the parent application), and which the Restriction Requirement of the Parent Application, by its own language, states as patentably distinct subject matter. As such, Applicants submit that the provisional rejection of claims 68-90 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 68, 138 and 143-153 of copending Application No. 09/932,677 is improper. Accordingly, Applicants request that this rejection be withdrawn.

Applicants further note that in copending Application No. 09/932,677, the provisional rejection of claims 68, 138 and 142-153 of copending Application No. 09/932,677 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims

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68-90 of U.S. Application No. 09/932,676 (the instant application) was withdrawn by the Examiner in the Office Action mailed from the U.S. Patent and Trademark Office on April 28, 2004, in light of similar remarks/arguments.

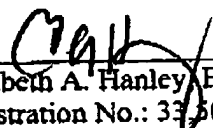
**CONCLUSION**

In view of the foregoing remarks, favorable reconsideration and withdrawal of the rejections, and allowance of this application with all pending claims are respectfully requested. If a telephone conversation with Applicants' attorney would expedite prosecution of the above-identified application, the Examiner is invited to call the undersigned at (617) 227-7400.

Respectfully submitted,

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